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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/547,447	08/26/2005	Andreas Renz	12810-00119-US	7056

23416 7590 12/11/2007

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	
MAIL DATE	**DELIVERY MODE**
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/547,447	RENZ ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *4,9-25 and 27-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-8 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 August 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/26/05 & 10/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's provisionally elected Group I, claims 1-3, 5-8 and 26, drawn to SEQ ID NO: 1, in the reply filed on 11/06/2007 is acknowledged. Applicants believe that there is no undue burden on the Examiner to search this invention.

In response, Examiner agrees with the Applicants that searching for one sequence is not a serious burden.

Claims 4, 9-25 & 27-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

2. Applicants' subsequent discussions indirectly traverse Examiner's lack of unity requirement and argue that unity of invention was found during the International stage. As shown in the International Preliminary Report on Patentability and International Search Report, all claims were searched and examined together. Thus, application of PCT Rules 13.1 and 13.2 by the International Examiners shows that unity exists. Since the search has already been conducted by the International Search Authority and the International Examination Authority and no lack of unity of invention has been found, for this additional reason, there would be no undue burden on the Examiner to examine all Groups in one application.

Additionally, unity of invention is further fulfilled because the claims are directed to a product and a process of use of said product, which are an acceptable combination of categories for unity pursuant to 37 CFR § 1.475(b)(3). Accordingly, Applicants respectfully request that the Examiner reconsider the restriction requirement and examine the claims in one application.

For the above reasons, Applicants respectfully request reconsideration and withdrawal of this restriction requirement

The argument is considered and found not persuasive because the technical feature linking Groups I-VI and (A)-(H) appears to be that they all relate to polypeptide having acyl-CoA:lysophospholipid-acyltransferase activity. According to the international preliminary examination report [IPER] clams 1-8, lack novelty as being anticipated by Accession No. Q22267; and claims 22-24 lack novelty as being anticipated by Heinz et al. [WO 01/59128 A, 8/16/2001]. Therefore, Groups I-VI and (A)-(H) share no special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The United Sates Patent and Trademark Office is not bound by the lack of unity determination by another International Searching Authority. MPEP 1875 states that whether or not the question of unity of invention has been raised by the International Searching Authority, it may be considered by the examiner when serving as an authorized officer of the International Preliminary Examining Authority. Thus, the Examiner is not bound by any previous determination made. In addition, 37 C.F.R. 1.484 indicates that the international preliminary examination is a non-binding opinion. Finally, 37 C.F.R. 1.499 states that, if the Examiner finds that a national stage application lacks unity of invention under 37 C.F.R. 1.475, the Examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Thus, the determination of lack of unity is proper under the PCT treaty.

The lack of unity determination is still deemed proper and is therefore made FINAL.

3. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

4. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in Germany on 2.27.2003.

5. ***Drawings***

Drawings filed 8/26/2006 is acknowledged. Brief description of drawings is missing from the specification. Correction is required.

6. ***Abstract***

*This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

*The abstract should be in narrative form and generally limited to a single paragraph within the range of 50 to 150 words [in length since the space provided for the abstract on the computer tape by the printer is limited]. The form and legal phraseology often used in patent claims, such as "means" and "said", should be avoided in the abstract. The abstract should sufficiently describe the disclosure to assist readers in

deciding whether there is a need for consulting the full patent text for details. MPEP 608.01(b).

The instant abstract is more than one paragraph and uses legal phraseology, such as 'said', for example. Correction is required.

7. ***Sequence Rules***

The instant specification on pages 44-45, present oligonucleotide; pages 50-51 & 58-59, Table 4 & 6 present primer sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but fails to comply with the requirements. According to 37 CFR 1.821-825, every disclosed amino acid sequence of four or more residues or 10 or more nucleotides must be identified by a SEQ ID NO. The nucleotide sequences presented do not have SEQ ID NOS. In order to comply with the sequence rules Applicants must identify these sequences by providing SEQ ID NO:, and where required provide a new version of the sequence listing and disk.

Applicant must submit a CRF copy and paper copy of the Sequence Listing, a statement that the content of the paper and computer readable copies are the same and where applicable include no new matter as required by 37 C.F.R. j 1.821(e) or 1.821(9 or 1.821(g) or 1 .825(d), as well as an amendment directing its entry into the specification. Appropriate corrections for compliance are required.

Specification

8. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

9. ***Claim Objections***

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 recite non-elected sequences, which must be deleted from the claims.

10. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Claims 1, 3, 5-8 & 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 & 3 are directed to a nucleic acid sequence encoding a polypeptide having acyl-CoA:lysophospholipid-acyltransferase activity with no defined structure of the nucleic acid. Claims 5-8 & 26 are directed to an gene construct comprising the nucleic acid sequence of claim 1 or is derived from eukaryote (claim 3). Claims 5-8 & 26 are rejected under this section of 35 USC 112 because the claim is directed to genomic DNA sequences not disclosed in the specification. No description has been provided of the genomic DNA sequences encompassed by the claim. Applicants have not adequately described the nature of the genomic DNA corresponding to the construct comprising the gene. No structural information, beyond the partial characterization by SEQ ID NO:[1 and 2] has been provided by Applicants which would indicate that they had

possession of the claimed genomic DNA, i.e. the gene corresponding to the disclosed cDNA sequences. Eukaryotic genes (genomic DNA sequences) are well known in the art of molecular biology to contain elements of structure not present in cDNA sequences. For example, introns are regions of DNA that interrupt coding sequences in eukaryotic genes. In different genes, introns have been detected that are as large as 2000 base pairs. Because cDNA libraries are generated by reverse transcription of mRNA which has been processed in the nucleus to remove introns, intron sequences are not present in cDNA libraries. Since the claimed genomic DNA has not been deposited and no other description of the claimed gene beyond that of the corresponding cDNA exists and no function has been determined aside from the assertion that the cDNA encodes a secreted protein, a person having ordinary skill in the art would not recognize that Applicants had possession of the claimed invention at the time of filing.

In Vas-Cath Inc. v. Mahurkar (CA FC) 19 USPQ2d 1111 the court held that:

Written description of invention required by first paragraph of 35 USC 112 is separate and distinct from that paragraph's requirement of enabling disclosure, since description must do more than merely provide explanation of how to "make and use" invention; applicant must also convey, with reasonable clarity to those skilled in the art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed.

Thus, while the argument may be made that claims 5-8 & 26 are enabled for an isolated gene corresponding to the cDNA

sequences of SEQ ID NO:[1 and 2], Applicants have not shown that they were in possession of the claimed gene at the time of filing. In Fiers v. Sugano, 984 F.2d 1164, 25 USPQ2d 1601, at USPQ2d 1606 the court stated: An adequate description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is description of the DNA itself.

Applicants have not adequately described the claimed gene because no information has been provided pertaining to sequences not present in the cDNA corresponding to the gene, these sequences may include introns as well as regulatory elements such as activators. To paraphrase the Court, if Applicants are unable to envision the detailed chemical structure of the claimed DNA then conception is not achieved until reduction to practice has occurred, that is, until after the gene has been isolated; thus, regardless of the complexity or simplicity of the method of isolation employed, conception of a DNA sequence, like conception of any chemical substance, requires definition of that substance other than by its functional utility.

Amending the claim to read "An isolated polynucleotide comprising..." or the like, would overcome this rejection.

The isolated nucleic acid of claim 1 or 3 completely lack structure. These claims are directed to a genus of DNA (or polynucleotide or nucleic acid) molecules wherein DNA sequence encodes a polypeptide having acyl-CoA:lysophospholipid-acyltransferase activity with no defined structure. The specification exemplifies SEQ ID NO: 1, which sequence is not representative of all the acyl-CoA:lysophospholipid-acyltransferase encoding nucleic acid from any source. The

specification discloses additional DNA sequence of SEQ ID No. 5 or 7 encoding the transferase enzyme of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

11. ***Enablement***

Claims 1-3, 5-8 & 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide (or nucleic acid or DNA) sequence of SEQ ID NO: 1, encoding a polypeptide having acyl-CoA:lysophospholipid-acyltransferase activity and the sequence of SEQ ID NO: 2, does not reasonably provide enablement for (1) a DNA encoding a polypeptide having acyl-CoA:lysophospholipid-acyltransferase with no defined structure; or (2) a DNA encoding a polypeptide which is at least 40% homologous to the amino acid sequence of SEQ ID NO: 2 and having acyl-CoA:lysophospholipid-acyltransferase activity; or (3) derivative of nucleic acid depicted in SEQ ID NO: 1; or (4) is a nucleic acid sequence which can be derived from the coding sequence of SEQ ID NO: 1, as a result of the degenerated genetic code.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a

protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide [SEQ ID NO: 1] and encoded amino acid sequence of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications or derivatization, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of DNA encoding SEQ ID NO: 2 by 60%, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting acyl-CoA:lysophospholipid-acyltransferase activity; (B) the general tolerance of acyl-CoA:lysophospholipid-acyltransferase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any lipid metabolism enzyme residues with an expectation of obtaining the

desired enzymatic or biological function capable of catalyzing a defined chemical reaction using known substrates; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the encoding DNA (or polynucleotide) encoding a specific acyl-CoA:lysophospholipid-acyltransferase of known substrate specificity having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

12. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 1, 3, 5-8 & 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 3-4, recites 'converts C_{16}, C_{18}-, C_{20}- or C_{22}-fatty acids'. It is unclear what the 'C_{16}, C_{18}-, C_{20}- or C_{22}-fatty acids' compounds are converted to ?? Clarification is requested.

Claims 3, 5-8 & 26 are included in the rejection for failing to correct the defect present in the base claim(s).

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5, 8 & 26 rejected under 35 U.S.C. 102(b) as being anticipated by Cases et al. (PNAS, USA, 95: 13018-13023, October 1998, cited PTO-1449). Cases et al. teach the Identification of a gene encoding an acyl CoA:diacylglycerol acyltransferase (also called lysophospholipid acyl transferase), a key enzyme in triacylglycerol synthesis. The reference teaches expression of the gene in suitable vector and host cells. The encoded enzyme uses fatty acyl CoA as a substrate. Expression of a mouse cDNA for this expressed sequence tag in insect cells resulted in high levels of DGAT activity in cell membranes. This is an enzyme known to act on C_{16}, C_{18}-, C_{20}- or C_{22}-fatty acids as substrate. The claims are written so broadly as to be anticipated by the reference.

14. Accession Number Q22267 (15 December 1998) is putative 1-acyl-sn-glycerol-3-phosphate acyltransferase (EC 2.3.1.51) enzyme and is 1005 identical to instant SQE ID NO: 2. The specific DNA encoding the protein (Q22267) is not known. The accession number, Q22267, is made of record here, but has not been used in any art rejection.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand

Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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December 3, 2007